Amendments to the Drawings:

The attached sheet of drawings includes changes to Figs. 3A and 3B. This sheet, which includes Figs. 3A and 3B, replaces the original sheet including Figs. 3A and 3B.

Attachment: Replacement Sheet

REMARKS/ARGUMENTS

Claims 1, 2, 5-7, 9, 10, 15-19 and 29-33 are pending. Claims 3, 4, 8, 11-14 and 20-28 have been cancelled. These claims have not been cancelled to avoid any reference but instead to expedite prosecution. The Applicant reserves the right to present these claims in a continuing application. Claims 1, 9, 10 and 15 have been amended. Claims 29-33 have been added. As detailed above, the specification and drawings have been amended. No new matter has been added with these amendments. In the Office Action, the Examiner rejected claims 1-19 on various grounds. The Applicant responds to each ground of rejection as subsequently recited herein. Reconsideration of this Application and entry of this Amendment is respectfully requested.

Specification Objections

The Examiner objected to the specification for improper claim identification. The Applicant has amended page 22 of the specification, changing the term "Claims" to "What is claimed is" as suggested by the Examiner.

Regarding the sequence listings, the Applicant has amended the specification to include a paper copy and a CRF copy of the sequence listings of FIGS 3A and 3B. A statement directing entry of the sequence listing into the specification is included. Further, a statement that the content of the paper copy and the CRF copy are the same is included in the attached appendix. The Detailed Description of the Drawings" has been amended to reference SEQ ID NO 1 and SEQ ID NO 2.

35 U.S.C. §112 Rejections

Claims 1-19 were rejected under 35 USC § 112, first paragraph for failing to comply with the enablement requirement. The Applicant respectfully traverses this rejection. The Applicant submits that the specification enables a person having ordinary skill in the art to practice the invention without undue experimentation.

The Examiner rejected the claims as nonenabling because the "claims read on administering any naked DNA or RNA or vector comprising a transgene encoding at least one protein. Independent claim 1 has been amended to include the limitation of "wherein the gene therapy agent comprises a vector selected from a group consisting of a plasmid, retrovirus vectors, adenovirus vectors, Herpes Simplex vectors, Semliki Forest Virus vectors, and Sindbis virus vectors and the at least one protein is chosen from a group consisting of a collagen isoform,

an A1 apolipoprotein isoform and an A1 apolipoprotein mutant Milano isoform" thereby obviating the rejection of independent claim 1 and all claims depending therefrom.

The Examiner further alleges that the specification fails to provide a correlation between the gene therapy agent encoding at least one protein and the vulnerable plaque associated with a blood vessel. This allegation is misplaced. The Applicant's specification at page 2 line 19 to page 3 provides correlation between the A1 apolipoprotein and A1 apolipoprotein mutant Milano isoform in conferring cardiovascular protection, citing several references to support the correlation. The Applicant further provides guidance regarding the use of collagen in modifying the fibrous cap, stating that the expressed collagen may reinforce or strengthen the fibrous cap thereby reducing the chance of rupture (see Applicant's specification page 11 lines 18-23).

The Examiner next alleges that the specification fails to provide adequate guidance and evidence for how to administer at least one gene therapy agent encoding at least one protein to treat a vulnerable plaque associated with a blood vessel. The Applicant respectfully draws the Examiner's attention to page 14 line 9 to page 17 line 11 and FIGS. 4 and 5 which provides a detailed example of administering a gene therapy agent as claimed by the Applicant.

The Examiner further alleges that it would have required undue experimentation for one skilled in the art at the time of the invention to practice over the full scope of the invention claimed. As noted above, independent claim 1 has been amended to more particularly point out and distinctly claim the Applicant's invention. The breadth of the amended claims are such that one of ordinary skill in the art could practice the invention without undue experimentation. The Examiner is correct in finding that the level of skill of one of ordinary skill in the art is high. Those with a heightened skill level are well aware of the experimental requirements of this field. As the Examiner is well aware, a high level of experimentation does not equate to undue experimentation where a high level of experimentation is typical within a particular field of endeavor and given the nature of the invention. One of ordinary skill in the art would not be unduly burdened when attempting to practice this invention particularly in light of the guidance provided in FIGS. 4 and 5 and the discussion of these figures. For at least these reasons, the finding by the Examiner that the Applicant's specification is not enabling can not be sustained. Thus, the Applicants respectfully request the withdrawal of the rejection of claims 1-19 under 35 USC §112, first paragraph.

35 U.S.C. §102 Rejections

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). The identical invention must be shown in as complete detail as is contained in the . . . claim. *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). Thus, to warrant the §102 rejections, the references cited by the Examiner must show each and every limitation of the claims in complete detail. The Applicant respectfully asserts that the cited references fail to do so.

A. Claims 1, 2, 4-7, 9, 15-17 and 19 were rejected under 35 U.S.C. §102(e) as being anticipated by U.S. Patent No. 7,008,411 to Mandrusov et al., (the Mandrusov patent).

The Applicant respectfully asserts that the Mandrusov patent fails to include each and every element of the Applicant's invention as claimed, as required to maintain a rejection under 35 U.S.C. §102(e). *See* MPEP 2131.

The Applicant asserts that the Mandrusov patent fails to disclose, teach, or suggest a method of treating a vulnerable plaque associated with a blood vessel of a patient that includes the steps of providing at least one gene therapy agent encoding at least one protein; administering the gene therapy agent to a target cell population; expressing the protein within the patient from a portion of the target cell population; and modifying the vulnerable plaque as a result of the protein expression, wherein the at least one protein is chosen from a group consisting of a collagen isoform, an A1 apolipoprotein isoform and an A1 apolipoprotein mutant Milano isoform, as recited in claim 1.

More specifically, the Applicant asserts that the Mandrusov patent fails to teach or suggest a method of treating a vulnerable plaque by modifying the vulnerable plaque with an expressed protein. Moreover, the Mandrusov patent fails to teach or suggest modifying the vulnerable plaque by the expression of at least one protein chosen from a group consisting of a collagen isoform, an A1 apolipoprotein isoform and an A1 apolipoprotein mutant Milano isoform.

At most, the Mandrusov patent teaches methods for treating a vulnerable plaque that include a therapeutic agent that may induce angiogenesis or arteriogenesis (see col. 4 lines 47-57) or that include a lipid lowering agent that may lower serum LDL cholesterol to increase the relative collagen content of the vulnerable plaque (see col. 6 lines 26-35). Thus, the Mandrusov patent does not teach Applicant's claimed method that includes "providing at least one gene therapy agent encoding at least one protein, modifying the vulnerable plaque as a result of the protein expression, wherein the at least one protein is chosen from a group consisting of a collagen isoform, an A1 apolipoprotein isoform and an A1 apolipoprotein mutant Milano isoform." For at least this reason, the Mandrusov patent does not anticipate claim 1. Claims 2, 4-7, 9, 15-17 and 19 depend directly or indirectly from independent claim 1 and include all of the limitations of that claim. For at least this reason, claims 2, 4-7, 9, 15-17 and 19 are allowable over the Mandrusov patent.

For these reasons, the withdrawal of the rejection of claims 1, 2, 4-7, 9, 15-17 and 19 under 35 U.S.C. § 102(e) is respectfully requested.

B. Claims 1-7, 9 and 15-18 were rejected under 35 U.S.C. §102(b) as being anticipated by WO 97/16169 to Hung et al., (the Hung patent).

The Applicant respectfully asserts that the Hung patent fails to include each and every element of the Applicant's invention as claimed, as required to maintain a rejection under 35 U.S.C. §102(b). *See* MPEP 2131. The Applicants assert that the Hung patent fails to disclose, teach, or suggest a method of treating a vulnerable plaque associated with a blood vessel of a patient that includes the steps of providing at least one gene therapy agent encoding at least one protein; administering the gene therapy agent to a target cell population; expressing the protein within the patient from a portion of the target cell population; and modifying the vulnerable plaque as a result of the protein expression, wherein the at least one protein is chosen from a group consisting of a collagen isoform, an A1 apolipoprotein isoform and an A1 apolipoprotein mutant Milano isoform, as recited in claim 1.

At most, the Hung patent teaches treating cardiovascular disease by delivering a therapeutic agent to the pericardial space. The Hung patent does not teach a method of treating vulnerable plaque. Consequently, the Hung patent does not teach modifying the vulnerable

plaque as claimed by the Applicant. Therefore, the Hung patent does not anticipate claim 1 or any claim depending therefrom. Claims 2-7, 9 and 15-18 depend from claim 1 and include all of the limitations of that claims. For at least this reason claims 2-7, 9 and 15-18 are allowable over the Hung patent. For these reasons, the withdrawal of the rejection of claims 1-7, 9 and 15-18 under 35 U.S.C. § 102(e) is respectfully requested.

New Claims are allowable

New claims 29-33 depend from independent claim 1 and include all of the limitations of that claim. For at least this reason, claims 29-34 are allowable over the cited art. Support for new claims 29-33 may be found at least at page 12 line 24 to page 13 line 11 and page 18 line 5 to page 19 line 9. The allowance of claims 29-33 is respectfully requested.

Conclusion

For the foregoing reasons, Applicant believes all the pending claims are in condition for allowance and should be passed to issue. The Commissioner is hereby authorized to charge any additional fees which may be required under 37 C.F.R. 1.17, or credit any overpayment, to Deposit Account No. 01-2525. If the Examiner feels that a telephone conference would in any way expedite the prosecution of the application, please do not hesitate to call the undersigned at telephone (707) 543-5484.

Respectfully submitted,

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